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MEDICAL IMAGING—RADIATION ONCOLOGY—ORIGINAL ARTICLE

Percutaneous microwave ablation for early-stage non-small cell lung cancer (NSCLC) in the elderly: A promising outlook

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Abstract

Introduction: Microwave ablation (MWA) is a relatively new minimally invasive treatment option for lung cancer with substantially lower morbidity and mortality than surgery. This retrospective study was performed to evaluate the safety, effectiveness and follow-up imaging of MWA in the elderly aged 75 years and above.
Methods: Eleven percutaneous computed tomography (CT)-guided MWA of early-stage non-small cell lung cancer (NSCLC) were performed in 10 patients aged 75 years and older. All but one patient were treated with a high-powered MWA system delivering maximally 140 W. Follow-up with CT and fludeoxyglucose-positron emission tomography (FDG-PET) was carried out over a maximum period of 30 months and a median period of 12 months.
Results: There were no peri-procedural deaths or major complications. Seven patients were disease free at the time of manuscript submission. Three patients showed growth of the treated lesions, one patient aged 90 years deceased due to unknown cause after approximately 18 months. One patient presented with local progression and disseminated metastatic disease at 12 months; he is still alive. One patient showed increasing soft tissue at the ablation site 15 months post-treatment. Three consecutive core biopsies over 2 months failed to confirm tumour recurrence.
Conclusions: MWA therapy is a promising option of treating early-stage NSCLC in the elderly with good treatment outcome and negligible morbidity. Determining successful treatment outcome may be challenging at times as local tissue increase and PET-CT positivity do not seem to necessarily correlate with reccurrence of malignancy.

Key words: elderly; lung cancer; lung tumour; microwave ablation; NSCLC; thermal ablation.

Introduction

Lung cancer is the leading cause of cancer death in Australia.[1] Survival rates for lung cancer remain poor despite recent advances in treatment. Eighty-five to ninety per cent of all lung cancers are NSCLC.[2] Surgery is the standard of curative therapy, but it is estimated that as many as 30% of patients over the age of 65 years diagnosed with early-stage NSCLC do not qualify for surgery due to medical comorbidities.[3] Over the past decade, thermal ablation has emerged as a viable alternative to surgery in a selected patient population, carrying lower morbidity and mortality. In lungs, microwave ablation (MWA) therapy is considered superior to other thermal ablation options, allowing for a more even, faster and deeper distribution of energy.[4] The purpose of this study was to retrospectively evaluate the safety and effectiveness of MWA and follow-up imaging in 10 patients aged 75 years and above with stage I NSCLC.

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Methods

Patients

Institutional ethics approval was obtained. We included the data of 10 patients (six men and four women) with 11 biopsy-confirmed NSCLCs treated with percutaneous CT-guided MWA. Mean age was 79 years (range 75–88 years). The patients were treated between September 2010 and October 2012. In patients 1, 5 and 10, increasing lesion size and fludeoxyglucose (FDG)-PET positivity post-radiotherapy were considered adequate evidence for local recurrence; repeat tissue sampling was performed in only one of these three patients. None of the included patients were surgical candidates due to medical comorbidities and high surgical risk (Table 1).

The lesions of patients 3 and 5 included in this study had already once been treated with MWA; both re-ablations were performed due to positive FDG-PET-CT scans within 6 months of the first ablation (Figs 1,2). Patient 2 had undergone radiofrequency ablation (RFA) of the target lesion 7 months prior to MWA; the re-ablation decision was also based on a 6-month PET positivity.

Tumour sizes ranged from 1.5 to 4.1 cm in maximal axial diameter. Ten of the 11 lesions were located in one of the upper lobes; one tumour was located in the middle lobe. All patients had pre-procedural PET scanning. All lesions but one, which was a small minimally invasive adenocarcinoma in patient 7, were FDG-PET positive.

Instrumentation

The ablations were performed under CT guidance (Philips Brilliance 64, Eindhoven, NL). All but one patient were treated with the Acculis microwave tissue ablation system (AngioDynamics, Latham, NY, USA), which operates at 2.45 GHz with a maximum power output of 140 W. The standard Accu2i pMTA applicator (AngioDynamics) with a 1.8-mm diameter, 14-cm shaft length and 16-mm active tip was used in all cases. The EvidentTM system (Covidien, Boulder, CO, USA), which operates at 915 MHz with a maximum power output of 45 W, was used in the remaining patient; a 13G antenna with a 2-cm active tip was used.

Procedure

All ablations were performed by the same interventional radiologist (KS, with 10 years of experience in image-guided thermoablative therapy). Patients were asked to stop anticoagulation therapy for 1–7 days pre-procedure, depending on the type of anticoagulation. Written informed consent was obtained. No prophylactic antibiotic treatment was administered. A non-contrast planning CT scan of the target area was performed immediately prior to the MWA. Patients received either conscious sedation or general anaesthesia. Under sterile conditions and CT guidance, the pMTA applicator was inserted into the target lesion. The final antenna position was confirmed on multiplanar reformats (Fig. 2a). Overlapping ablations were performed if considered appropriate, usually in lesions with a diameter larger than 3.5 cm. The lesion size, shape and proximity to vessels dictated the ablation parameters, with power output and ablation duration chosen and adjusted accordingly. Total ablation time ranged between 2.5 and 10 minutes. Except for the ablation with the Evident system at 45 W, the power used ranged between 80 and 100 W. Technically successful ablation was defined as completed planned ablation cycle(s) and circumferential perilesional ground glass opacity (GGO).

Post-procedural management and follow-up

Three hours post–MWA, a chest X-ray was performed to check for post-procedural complications.

Table 1. Patient and tumour characteristics

Patient	Age	Sex	Previous treatment	Co-morbidities
1	88	M	No	Aortic stenosis, atrial fibrillation, IHD, cognitive impairment, vitamin B12 deficiency, glaucoma, gout, dementia
2	81	F	RFA	IHD and CABG, AAA 5.5 cm, post-nephrectomy (RCC and structural hydronephrosis)
3	79	M	MWA	Prostate cancer (1994) with bony metastases, HTN
4	75	F	No	Breast cancer (2011), vascular co-morbidities
5	76	F	Conservative radiotherapy and MWA	IHD and CABG
6	76	M	Conservative radiotherapy	Bronchiectasis with chronic pseudomonas and aspergillus colonisation, Barrett's oesophagus, COPD
7	75	F	No	Multifocal bronchoalveolar carcinoma
7	75	F	No	Multifocal bronchoalveolar carcinoma
8	80	M	No	Asbestosis, COPD, hyperlipidaemia, glaucoma
9	88	M	No	Rheumatoid arthritis, COPD, osteoporosis, peptic ulcer disease, TKR with peri-prosthetic fracture prior to MWA
10	75	M	Conservative radiotherapy	Bilateral iliac stent, DM, CABG, HTN, GORD, COPD, sleep apnoea

AAA, abdominal aortic aneurysm; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; F, female; GORD, gastro-oesophageal reflux disease; HTN, hypertension; IHD, ischaemic heart disease; M, male; MWA, microwave ablation; RCC, renal cell carcinoma; RFA, radiofrequency ablation; TKR, total knee replacement.

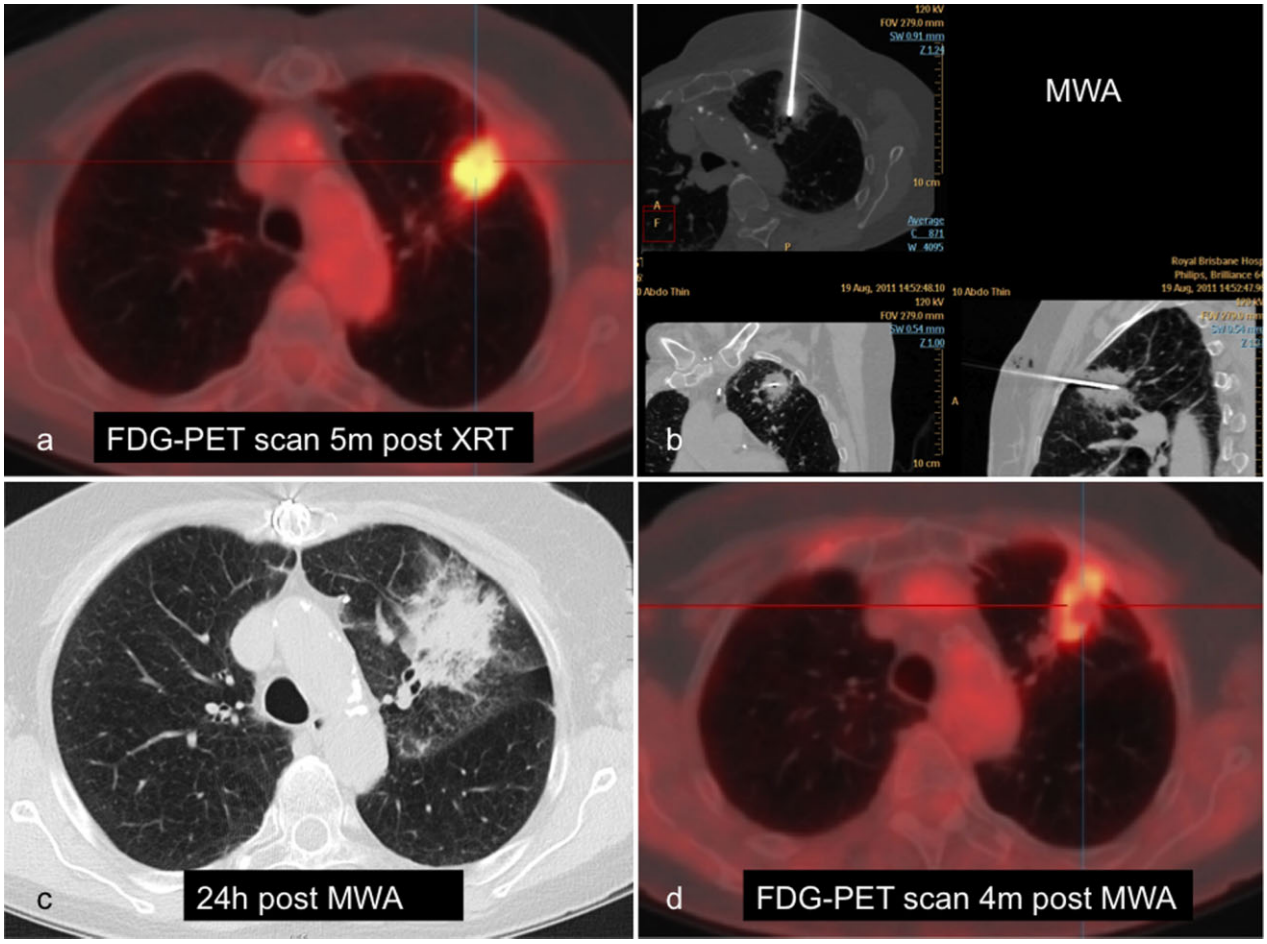

Fig. 1. Seventy-five-year-old female post-radical external beam radiation (XRT) for left upper lobe T1N0M0 non-small cell lung cancer (NSCLC): (a) fludeoxyglucose (FDG)-positron emission tomography (PET) scan 5 months post-conclusion of XRT shows residual local tumour avidity; (b) microwave ablation (MWA), multiplanar reformats show central position of the antenna within the tumour; (c) axial CT scan lung window 24 hours post-MWA shows the ablated tumour surrounded by ground glass opacity (GGO); (d) FDG-PET scan 4 months post-MWA shows residual ring-like uptake, reported as residual/recurrent local disease.

A non-enhanced CT scan of the ablation site was performed 24 hours later to assess the thermal damage and check for subtle complications. It also served as the baseline scan all future imaging would be compared against.

Further CT follow-up imaging was performed at 3, 6 and 12 months post-ablation and 6 monthly scans thereafter. As the majority of the patients came from outside our hospital's catchment area, their follow-up imaging was performed on different scanners, using different protocols and reconstruction algorithms. FDG-PET scan was performed 3–12 months post-ablation therapy whenever possible. Local recurrence of disease was defined according to the modified response evaluation criteria in solid tumors (RECIST) criteria (Table 2), factoring in not only the size of the ablated lesion, but also the mass quality and the FDG-PET avidity.[5]

Results

Short-term treatment outcome: successful ablation and adequacy of treatment

Altogether, 11 MWA sessions were performed in 10 patients. The procedure was presumed technically successful if correct positioning of the MWA applicator within the target lesion was achieved and the ablation cycle was completed as planned. One ablation attempt (patient 7) had to be aborted due to peri-lesional alveolar haemorrhage upon advancement of the antenna, masking the target lesion and precluding precise positioning of the antenna. The patient had some haemoptysis which settled quickly, she remained asymptomatic and was discharged the day after. The ablation was successfully performed 1 month later. Patient 10, with a large local recurrence post-conventional external beam radiation

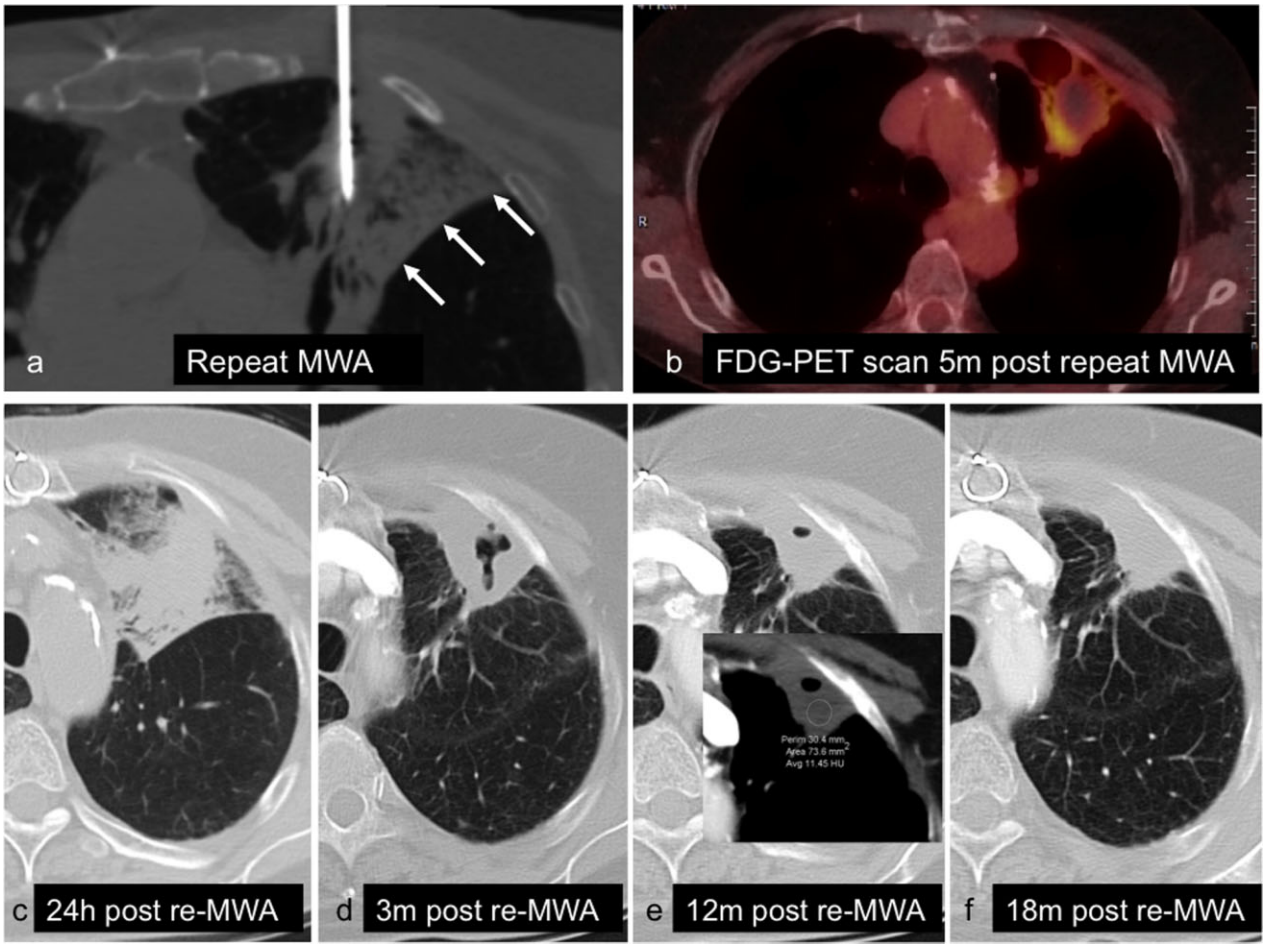

Fig. 2. Seventy-five-year-old female with microwave ablation (MWA) of local recurrence post-radical external beam radiation (XRT) for left upper lobe T1N0M0 non-small cell lung cancer (NSCLC). (a) Repeat CT-guided MWA, axial plane. Intra-procedural haemorrhage (arrows) (b) fludeoxyglucose (FDG)-positron emission tomography (PET) scan 5 months post-repeat MWA shows residual medial uptake deemed equivocal. (c–f) Axial CT scans between 24 hours and 18 months post-re-ablation show gradual shrinkage of the ablated focus; tissue density of 11 HU on the 12-month scan (inset) reflects no residual enhancement.

(XRT) and extensive comorbidities (Table 1), suffered from intractable cough throughout the first ablation cycle, which was eventually completed, with a central and a proximal ablation performed. An initially intended repositioning and further overlapping ablation was not carried out due to the patient's ongoing cough. The control scans post-ablation showed a medium-sized pneumothorax and moderate surgical emphysema.

Table 2. Modified RECIST criteria to evaluate treatment response post-thermal ablation

Response	CT mass size (RECIST)	CT mass quality	FDG-PET (SUV uptake)
Complete (any two)	Lesion disappearance or scar <25% original size	Cyst or cavity formation; low density of entire lesion	SUV < 2.5
Partial (any one)	Decrease by >30% in LD of target lesion	Central necrosis or central cavity with liquid density	Decreased SUV compared with baseline
Stable disease (any one)	Decrease by <30% in LD of target lesion	Solid mass, no central necrosis or cavity	Unchanged SUV compared with baseline
Progression (any two)	Increase by >20% in LD of target lesion	Solid mass, invasion of adjacent structures	Increased SUV compared with baseline

Target lesions are tumours treated with MWA. FDG, fludeoxyglucose; LD, largest diameter of target lesions; PET, positron emission tomography; RECIST, response evaluation criteria in solid tumours; SUV, standard uptake value of FDG F18 in PET scan.

Successful and complete treatment was thus achieved in all ablation sessions but one.

The mean ablation time for the lesions treated with 80–100 W was 3 minutes and 58 seconds (Table 3).

After MWA, GGO was apparent in nine of the treated lesions (82%); one did not show GGO, and one CT scan was not interpretable due to peri-lesional haemorrhage. Circumferential GGO was observed in five patients (46%) (Table 3).

Short-term treatment outcome: side effects and complications

Immediate, peri-procedural and delayed complications were recorded on a per-treatment basis and were classified in accordance with the Common Terminology Criteria for Adverse Events of the National Cancer Institute.[6] There were no intra-procedural or 30-day post-procedural deaths. Of the 11 microwave sessions, nine were accompanied by complications (82%), which were mostly minor in nature (Table 4). Bleeding occurred mainly along the applicator track. Length of admission ranged between 1 and 8 days (Table 3). Two patients who had predisposing co-morbidities (one with chronic pseudomonas colonisation on the background of bronchiectasis, one with asbestosis) developed short-term infective symptoms which resolved with oral antibiotic treatment. The most unusual complication was the loss of the ceramic tip coating in the pleural cavity while withdrawing the antenna, which did not cause symptoms or have other consequences for the patient.[7]

Long-term treatment outcome

All treated lesions were followed up by CT scans, and most were also followed by FDG-PET scans. Size and characteristics of the ablated tumour were determined according to modified RECIST criteria,[5] factoring in the size, quality of the ablated focus and FDG uptake characteristics, and compared with the size of the treated lesion 24 hours after MWA.

The minimum and median CT follow-up in all patients was 12 months, while the longest follow-up was 30 months (Table 3). At the time of manuscript submission, patient 9 had died at age 90, 19 months post-ablation, with local recurrence at the treatment site. He was without evidence of distant disease, and the death was more likely related to his total knee replacement and periprosthetic fractures complicated by osteomyelitis. All other patients were alive, of whom patient 10 had unequivocal progressive disease (PD). According to the modified RECIST criteria, three patients showed complete response (CR), and five showed partial response (PR, Table 3). All of the patients counted as showing PR did actually have no convincing sign of residual or PD; they however did not meet two of the three required criteria for CR, none of them having decreased in size to 25% or below of the original size. The most notable outcomes were as follows:

An increase in tumour size beyond the 24-hour scan was noticed in three of the 11 lesions (patients 8, 9 and 10). Of these, only patient 10 had local and distant disease recurrence. This patient had the largest lesion (4.1 cm prior to ablation) and had had prior XRT, and only an incomplete ablation had been carried out due to intractable cough throughout the procedure.

Patient 8 had a positive CT and FDG-PET scan 15 months post-ablation; three following CT-guided core biopsies, each 1 month apart, did not confirm the presence of cancerous cells. Only inflammation, granulation tissue and neo-angiogenesis were found. Despite the significant increase of the treated lesion in this patient, recurrence was histologically ruled out. The lesion is now decreasing in size and is displaying cavitation. The patient remains asymptomatic 30 months after therapy (manuscript to be submitted separately after the 36-month scan).

Only two of the ablated lesions that progressively decreased in size beyond the 24-hour scan became smaller than the pre-MWA within the first year (patients 7 and 8). None of the lesions disappeared or featured as a linear scar only.

PET-CT follow-up was performed for nine of the 11 lesions, 3–12 months after MWA therapy. FDG uptake in the area of the original lesion was noted in five patients. Regional or distant increased uptake was noted in three patients; only one patient with bony metastasis had both local and distant uptake (Table 5). An avid rim of FDG uptake can be often seen around the ablation zone for up to 6 months post-ablation, usually indicating reactive and inflammatory changes only (Fig. 2).[8]

Discussion

Globally, the mortality of lung cancer continues to increase, with 1.2 million deaths reported in 2000 and 1.5 million deaths in 2011.[9] The risk of contracting lung cancer rises with age, with 85% of all newly diagnosed lung cancer patients being 60 years and older.[1]

Gold standard for treatment is surgical resection. Surgery poses major risks with a 2–3% operative mortality for patients aged 70–79 years.[10] Finlayson *et al*. found that 93% of patients aged 65–69 years were discharged back home after cancer surgery, while only 75% of patients aged 80 years or older could be discharged home, with the remainder requiring transfer to other facilities like nursing homes.[11]

RFA has been offered as an alternative treatment option for early-stage NSCLC for well over a decade with promising mid- to long-term results in tumours smaller than 3 cm.[12,13] MWA should theoretically be superior to RFA in lungs because it is not limited by factors such as

Table 3. Treatment outcome: pre-ablation measurements, CT follow-up results and survival status of patients

Patient	Tumour size pre-MWA (cm)	Tumour size 24 h post-MWA (cm)	GGO 24 h post-MWA	cGGO 24 h post-MWA	Tumour size 3 m post-MWA (cm)	Tumour size 6 m post-MWA (cm)	Tumour size 12 m post-MWA (cm)	Tumour size 18 m post-MWA (cm)	Tumour size 24 m post-MWA (cm)	Tumour size 30 m post-MWA (cm)	Power and duration of ablation for each application	Length of admission (days)	Local control rate	Survival status
1	2.0	4.1	Yes	Yes	–	–	2.5↓	2.3↓	2.0↓	–	100 W, 3 min 0 s	1	PR	Alive
2	2.9	3.7	Yes	Yes	3.6↓	3.6↓	3.6↓	–	2.4↓	2.3↓	90 W, 3 min 30 s	1	CR	Alive
3	2.3	2.9	Yes	No	–	2.8↓	2.5↓	–	–	–	90 W, 3 min 10 s	5	PR	Alive
4	1.7	2.9	Yes	No	2.2↓	2.2↓	1.7↓	1.3↓	–	1.0↓	45 W, 10 min 0 s	1	CR	Alive
5	2.8	4.6	NA†	NA†	4.5↓	3.6↓	3.2↓	2.8↓	–	–	100 W, 3 min 0 s 100 W, 2 min 0 s	1	PR	Alive
6	3.3	5.0	Yes	Yes	5.0↓	4.0↓	3.5↓	–	–	–	100 W, 4 min 0 s	1	PR	Alive
7	2.8	5.5	Yes	Yes	3.5↓	3.1↓	1.9↓	–	–	–	90 W 3 min 20 s	1	CR	Alive
7	1.1	3.5	NA†	NA†	2.5↓	2.1↓	1.9↓	–	–	–	90 W, 1 min 30 s	1	PR	Alive
8	2.6	3.4	Yes	Yes	3.6↑	–	2.5↓	4.7↑	4.4↓	5.5↑	80 W, 4 min 0 s 100 W, 2 min 0 s	8	PD‡	Alive
9	3.6	4.5	Yes	No	3.5↓	–	–	5.0↑	–	–	80 W, 1 min 20 s 90 W, 3 min 0 s	5	PD	Dead
10	4.1	6.2	Yes	No	3.8↓	3.5↓	4.5↑	–	–	–	90 W, 4 min 15 s 100 W, 1 min 30 s	1	PD	Alive

Tumour size was determined by measuring the longest axial diameter. Additionally, the treatment duration, used power output, length of admission, local control rate and survival status are indicated. The arrows indicate whether the lesion has grown (↑) or decreased in size (↓) compared with the previous CT. The '–' symbol indicates that a control scan was not performed or not performed yet at that point in time. †GGO masked by peri-lesional haemorrhage. ‡Increase in size and FDG-PET avidity; PD could however not be verified on three core biopsies, one month apart, of the PET-avid tissue. cGGO, circumferential ground glass opacity; CR, complete response; FDG, fludeoxyglucose; GGO, ground glass opacity; MWA, microwave ablation; NA, not applicable; PD, progressive disease; PET, positron emission tomography; PR, partial response.

Table 4. Complications

Complications	Absolute	Percentage of ablations	CTCAE grade
Pneumothorax (mild)	5	45.5	1
Pneumothorax requiring chest tube	3	27.3	2
Chest wall burn	1	9.1	1
Infection	2	18.2	2
Haemoptysis	1	9.1	1
Alveolar haemorrhage	5	45.5	1
Surgical emphysema	2	18.2	1
Loss of ceramic coating tip of antenna in pleural space	1	9.1	1

CTCAE, Common Terminology Criteria for Adverse Events of the National Cancer Institute.

non-continuous delivery of heat through different tissues, dependency on tissue conductivity, significantly longer ablation times, heat sink effect, higher intra-procedural pain, pacemaker interference and the need for grounding pads with the potential complication of skin burns, just to name a few.[14–17]

Conventional XRT, traditionally used for the treatment of NSCLC in non-surgical candidates, including early stages, has been widely abandoned and replaced by stereotactic body radiation therapy (SBRT) in early-stage node-negative NSCLC. Wisnivesky *et al*. assessed the outcome of 4357 stage I and II NSCLC patients, 88% of whom were stage I, who weren't surgical candidates and received either conventional radiotherapy or observation only. In the two groups, the median survival time for patients with stage I disease differed by 7 months, for stage II disease by 5 months, and there was no survival difference at 5 years (11% vs 10%).[18]

SBRT is at present considered the gold standard for non-surgical treatment of node-negative small NSCLC,[19,20] also specifically addressing the elderly as a suitable target population.[21,22] Unfortunately, despite having the required equipment at our hospital, we are unable to offer SBRT to our lung cancer patients on a routine base. While the acute complications of MWA appear to outweigh those of SBRT, owing to the invasive nature of MWA, this relation reverses in the chronic setting, MWA being virtually devoid of complications such as radiation toxicity, chest (wall) pain beyond the acute phase, chronic cough and rib fractures.

MWA possesses many advantages compared with other therapy options for lung cancer treatment; it is a well-tolerated procedure, which makes it especially suitable for elderly patients. The 30-day mortality for MWA has been reported as exceedingly low.[23–26] Our study supports this experience in elderly patients. The most common complications for MWA are small pneumothoraces, usually self-limiting. None of the patients in the presented cohort developed a pleural effusion large enough to be symptomatic and require drainage. Furthermore, MWA therapy sessions are very short. The mean treatment time for our 80–100 W sessions was 3 minutes and 58 seconds, which includes

Table 5. FDG-PET follow-up

Patient	PET post-MWA (months)	FDG uptake locally, report	FDG uptake regionally or distantly, report
1	12	No FDG uptake	FDG uptake in the ascending colon: likely due to a polyp
2	6	FDG uptake in the periphery of the left upper lobe lesion, retrospectively inflammatory as lesion continued to shrink	No FDG uptake
3	6	No FDG uptake	No FDG uptake
4	8	No FDG uptake	FDG uptake in ipsilateral hilar lymph nodes, retrospectively inflammatory
5	6	FDG uptake: residual/recurrent tumour or inflammatory change	FDG uptake in ipsilateral hilar lymph nodes, retrospectively inflammatory
6	–	–	–
7	8	FDG uptake: residual/recurrent tumour or inflammatory change	No FDG uptake
7	8	PET neg	No FDG uptake
8	3, 15	FDG uptake: local recurrence; three biopsies on three different days showed inflammation only	No FDG uptake
9	–	–	–
10	4	FDG uptake: residual disease likely	FDG uptake in right clavicle

FDG, fludeoxyglucose; MWA, microwave ablation; PET, positron emission tomography; –, not performed.

overlapping ablations. This is significantly faster than MWA with a low power technique of 45–60 W.[24–26]

Patients can be treated as outpatients or be kept overnight, which allows for higher quality of recovery of the patient in familiar surroundings, with reduction in treatment and overall costs compared with surgical management or radiotherapy.[27]

Another major advantage of MWA is the option to repeat the treatment as often as indicated,[28] an option radiation therapy is lacking. Three of our patients received repeat ablation for suspected local recurrence.

Correct determination of disease recurrence is difficult. Regrowth of tissue at old tumour sites is not necessarily due to recurrence of disease, as shown in patient 8 who had three core biopsies of the FDG-PET avid growing lesion, showing no evidence of malignancy. Thirty months post-therapy, the lesion is stable and shows central cavitation, which has been described with improved survival rates.[25] Similarly, FDG uptake at ablated tumour sites is not necessarily associated with recurrence of disease. Wolf *et al*. described lymphadenopathy to be a poor marker for progression of malignancy post-MWA.[25] The assumption that such changes might reflect inflammatory response mimicking recurrence of malignancy is supported by the histological findings of patient 8, which showed inflammatory cells only. In contrast, reduction in size of the treated lesion cannot be taken as guarantee for disease regression or eradication. Patient 10 continued to show a continuous decrease in size of the treated lesion at 6 months post-therapy, owing to collapse of central necrosis, but has unequivocal residual peripheral disease and has developed disseminated metastatic disease since.

Taking these aspects into consideration, in equivocal cases, only biopsy can reliably determine whether local disease has been eradicated or not. Sofocleous *et al*. have also postulated that RECIST criteria alone appear to be suboptimal in determining successful treatment of thermally ablated lung tumours.[8]

Interestingly, very few of the treated lesions that showed reduction in size beyond the 24-hour scan were at 12 months smaller than the target lesion prior to ablation.

MWA therapy appears to be a promising way of treating early-stage NSCLC, especially in patients not suitable for surgery, such as elderly patients.

Direct comparison of MWA therapy to surgical therapy will remain difficult as usually only patients unfit for surgery or who request MWA will be offered ablation therapy, this bias likely impacting survival figures. Also, realistically, multi-centre prospective randomised trials comparing SBRT with thermal ablation/MWA are unlikely to happen any time soon, not least because of, at least in Australia, too few centres offering both treatment modalities. A recent article comparing SBRT with image-guided thermal ablation for early-stage NSCLC concludes that there is no difference in survival outcome between the two modalities.[27] SBRT has been around for long enough to prove itself to be significantly superior to conventional external beam radiation for early-stage NSCLC and worthy as a viable alternative to surgery. MWA is in its infancy; however, the mid-term data and outlook are promising.

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